## REMARKS

Claims 1-38 are pending in the instant application. Claims 39-46 have been added. Accordingly, following entry of the present amendment, claims 1-46 will be pending.

The new claims are directed to a pharmaceutical composition comprising a gold compound and one or more corticosteroids selected from the group consisting of fluocinolone acetonide and mometasone furoate, in combination with a pharmaceutically acceptable carrier, excipient, adjuvant or solvent. Further new claims are directed to methods of treating an immune-mediated disorder comprising administering to a patient in need of such treatment a pharmaceutical composition as mentioned above. Accordingly, the new claims are collectively drawn to particular combinations of gold compounds and corticosteroids, and uses thereof.

Support for the new claims can be found throughout the specification and the claims as originally filed. In particular, the specification teaches combinations of corticosteroids and gold compounds as claimed that are selected to treat a particular manifestation of an immune disease, as described, for example, at page 3, lines 4-8; in Example 4; at page 22, lines 18-20; at page 23, paragraphs 2 and 3; and at page 24, paragraphs 1 and 2. The new claims have further basis in the data summarized in Tables 9 and 10 and depicted in Figures 1 and 2, teaching specific combinations of gold and corticosteroid that are particularly effective in the treatment of cell hyperproliferation (*e.g.,* gold and fluocinolone acetonide) or inflammation (*e.g.,* gold and mometasone furoate), two primary manifestations of immune disease.

No new matter has been added. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

### *Withdrawal of Certain Rejections*

Applicants gratefully acknowledge the Examiner's withdrawal of the following rejections:

1. The rejection of claims 1-5, 7-8, 11-15, 18, 21, 22, 27 and 29-37 under 35 USC 102(b) over Papandrea (AU-34351/89).
2. The rejection of claims 1-5, 7-8, 11-15, 18, 21, 22, 27 and 29-37 under 35 USC 102(b) over Papandrea (US 5,527,779).

3. The rejection of claims 1-37 under 35 USC 103(a) over Papandrea (AU-34351/89 or US 5,527,779).

***Rejection of Claims 1–38 Under 35 U.S.C. § 112***

The Examiner has rejected claims 1-38 under 35 U.S.C. §112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of filing, had possession of the claimed invention". Specifically, the Examiner is of the opinion that while the instant claims recite a "method of selecting a treatment", the specification does not describe a "selection process". The Examiner further states that "the pages and lines of the present specification indicated by applicant provide support for a method of treating an immune-mediated disorder and not a method of selecting a treatment for an immune-mediated disorder".

Applicants respectfully traverse this rejection. As described in detail in Applicants' specification, the present invention is based on the unexpected finding that particular corticosteroids exhibit synergistic activity with gold compounds towards specific manifestations of an immune-mediated disorder. With some corticosteroids, the synergy exhibited is toward the inflammatory components of the disease only, and with others it is toward the cellular hyperproliferation only. Accordingly, one fundamental aspect of the invention, that would be clearly apparent to one of ordinary skill in the art based on Applicants' specification, is the selection of particular treatments for immune mediated disorders having an inflammatory component and/or a cellular hyperproliferation component. As described and exemplified in Applicants' specification, this can be achieved by identifying the presence of one or both of the components of the immune disorder; and then selecting at least one corticosteroid which interacts with a gold compound to exhibit preferential synergistic action towards the one component of the disorder if only one component is present, or to exhibit equal action towards each component of said disorder if both components are present. Accordingly, Applicants' specification contains more than sufficient written description to inform one of ordinary skill in the art that Applicants had possession of the claimed invention at the time the application was filed, as required under §112, first paragraph (see MPEP 2163.02).

The fundamental factual inquiry in a written description rejection is whether the claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim ***need not be described literally*** (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. MPEP 2163.02. Rather, the inquiry into whether the written description requirement is met must be determined on a case-by-case basis and is a question of fact. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Moreover, the Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *In re Wertheim* 541 F.2d 257, 265, 191 USPQ 90, 98 (CCPA 1976); *Ex parte Sorenson*, 3 USPQ2d 1462, 1463 (BPAI 1987). MPEP 2163.04.

Applicants' specification satisfies the foregoing requirements for the presently claimed invention. In particular, the specification teaches how to identify which arm of the immune disorder (*e.g.*, inflammation and/or cell hyperproliferation) is being manifested, and how to select an effective gold/corticosteroid combination (e.g., exhibiting synergy) for treating the manifested condition, such that it would be clear to a skilled artisan that Applicants had possession of the invention at the time of filing. For example, the specification states on page 2, paragraph 5, that "The present invention is based on a surprising finding that important differences exist between corticosteroids with respect to the degree of potentiation of effects and the type of effect potentiated, when combined with a gold compound." It is further stated on page 3, lines 4-8, that "In the compositions of the present invention certain corticosteroids synergize with the gold compound to provide a greater effect on the inflammatory component of a disorder, such as psoriasis, while other corticosteroids give rise to compositions with preferential effects on cellular hyperproliferation." These statements clearly and obviously imply that the invention includes the selection of corticosteroid/gold compound combinations that produce a desired effect in the treatment of a specific manifestation of an immune-mediated disorder (*e.g.*, psoriasis). Accordingly, based on these statements, it would be clear to one of ordinary skill in the art that Applicants had possession of the invention at the time of filing. Indeed, as noted above, the claimed subject matter ***need not be described literally*** to satisfy the written

description requirement, as long as the description clearly conveys the invention to those skilled in the art. The present description does this.

Further written description supporting the pending claims is found in particular embodiments of the described invention, for example, at pages 3-5. In particular, page 4, paragraph 3, teaches that a corticosteroid can be ***selected*** to provide a synergistic composition with ***preferential action towards the inflammatory*** component, and that a second corticosteroid is ***selected*** to provide a synergistic composition with ***preferential action towards the cellular hyperproliferation*** component of a disorder. Further, it is stated on page 4, lines 31-32, that "The corticosteroid can be ***selected*** to provide a synergistic composition with activity towards ***cellular hyperproliferation in preference to inflammation or vice versa***." These statements clearly teach that a ***selection*** can be made not only in the choice of corticosteroid, but also in the choice of the component of the disorder to which the corticosteroid combination is to be applied.

Further support for and use of the term "selection" can be found in the description of various aspects and preferred embodiments on page 5. In addition, Applicants' specification provides working examples demonstrating and involving the actual selection of treatments, *e.g.*, preferred gold/corticosteroid combinations. In particular, Examples 2-4 (pages 12-24) teach how to select treatments using mouse models in which the presence of one or more components of an immune disorder (*i.e.*, an inflammatory component and/or a cellular hyperproliferative component) have been identified. Specifically, the presence of either epidermal hyperplasia, dermal inflammatory cell infiltration, or both of these components, was identified in TPA treated mice. As described in Example 4 (listed as Figure 2), the effects of various combinations of corticosteroids and gold compounds were tested for their efficacy in treating one or both of the components (see, *e.g.*, page 3, line 1; page 14, lines 8-10; page 22, lines 18-24; and page 23, lines 29-33). The data provided in Example 4 (summarized in Tables 9 and 10 and depicted graphically in Figures 1 and 2) shows a striking synergism between auranofin and particular, but not all, corticosteroids towards one or the other manifestation of an immune-mediated disorder. Indeed, on page 22, last paragraph, it is stated that: "With respect to effects on epidermal hyperplasia only two of the four steroids tested could be regarded as showing a synergistic reaction with auranofin." Similarly, it is stated on page 23, paragraph 3: "With respect to inflammatory cell infiltration into the dermis, the results in Table 10 indicate that the effect of

combination of auranofin (0.2%) and mometasone furoate is the result of synergism since the apparent $IC_{50}$ is increased by about 3,800%."

Accordingly, the foregoing Examples clearly teach the selection of specific gold/corticosteroid combinations useful for treating a particular manifestation of an immune-mediated disorder, as presently claimed. Examples 2-4 illustrate, by way of actual studies, how to test and identify (*i.e.,* select) a gold/corticosteroid combination for treating a particular manifestation of an immune-mediatd disorder, *e.g.*, cell hyperproliferation and/or inflammation. Thus, Applicants' specification clearly conveys to those of ordinary skill in the art that Applicants had possession of the claimed methods for selecting immune disorder treatments.

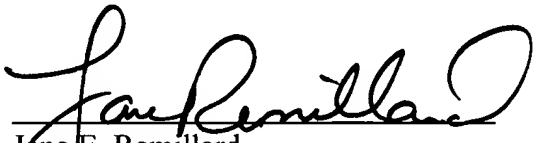
Accordingly, for at least the foregoing reasons, Applicants respectfully submit that the rejection of the claims for lack of Written Description should be withdrawn. Moreover, the Examiner has not provided sufficient evidence or reasons why one of ordinary skill in the art would not recognize in the instant specification that Applicants had possession of the claimed method of "selecting a treatment". Applicants maintain that there is sufficient description in the instant specification for the pending claims. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-38 under 35 U.S.C. §112, first paragraph.

## CONCLUSION

Reconsideration and allowance of all the pending claims is respectfully requested. If a telephone conversation with Applicants' attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 227-7400.

Respectfully submitted,

LAHIVE & COCKFIELD, LLP



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